



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/826,206	04/05/2001	John D' Elia	1533.1100001/MAC/DJN	2584
28393	7590	12/19/2003	EXAMINER	
STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C. 1100 NEW YORK AVE., N.W. WASHINGTON, DC 20005			RAO, MANJUNATH N	
			ART UNIT	PAPER NUMBER
			1652	

DATE MAILED: 12/19/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/826,206	Applicant(s) D' ELIA, JOHN	
	Examiner Manjunath N. Rao, Ph.D.	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) ____ is/are pending in the application.
 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 a) ☐ All b) ☐ Some * c) ☐ None of:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
 * See the attached detailed Office action for a list of the certified copies not received.
- 13) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
 a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). ____ . |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ . | 6) <input type="checkbox"/> Other: _____ . |

Art Unit: 1652

DETAILED ACTION

Claims 1-39 are currently pending and are present for examination.

Applicants' amendments and arguments filed on 9-17-03, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2, 4-39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide having the function of a replicon, i.e., capable of replicating itself in a bacterial cell, does not reasonably provide enablement for using any polynucleotide comprising a polynucleotide having a nucleotide sequence that is at least 95% identical to *Ketogulonigenium* plasmid replicon comprising SEQ ID NO:1, 3, or 4 or further comprising any other polynucleotide or any temperature sensitive replicon. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the

Art Unit: 1652

prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-2, 4-39 are so broad as to encompass any or all polynucleotides comprising a polynucleotide that is 95% identical to SEQ ID NO:1, 3, or 4 and further comprising other nucleic acid sequences such as mob sites, cos sites, marker genes etc. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the nucleotide sequence determines the amino acid sequence of the encoded protein which in turn determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence (i.e., which codons encoding the respective amino acids), if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide sequences of SEQ ID NO:1, 3 and 4 having the replicon function. It would require undue experimentation of the skilled artisan to make and use the claimed polypeptides with an undefined function/activity. The specification is limited to teaching the use of polynucleotides comprising SEQ ID NO:1, 3 and 4 as replicons in certain bacterial cells but provides no guidance with regard to the making of variants and mutants and with regard to uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polynucleotides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polynucleotide/polypeptide primary structure (e.g., see Ngo et al. in

Art Unit: 1652

The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), the claimed invention would require undue experimentation in order to determine its use. As such, the specification fails to teach one of ordinary skill how to use the full scope of the polypeptides encompassed by this claim.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made by altering the codons on the encoding polynucleotide with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide with 95% identity to the SEQ ID NOS:4 and because the specification does not establish: (A) a rational and predictable scheme for using polynucleotides that are 95% identical to SEQ ID NO:4 (claim lacks function of the claimed polynucleotide); (B) regions of the polynucleotide structure which may be modified without affecting its activity; (C) the general tolerance of such polynucleotides to modification and extent of such tolerance; (D) a rational and predictable scheme for modifying any nucleotide with an expectation of obtaining the desired biological function; and (E) the specification

Art Unit: 1652

provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides with an enormous number of amino acid modifications of SEQ ID NOS:1, 3 and 4 without providing its function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of polynucleotides having the desired biological characteristics and using such polynucleotides for a specific function is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim 1 and claims 2, 4-39 which depends therefrom are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules comprising any DNA which is 95% identical to SEQ ID NO:4.

The specification does not contain any disclosure of the function of all DNA sequences that are 95% identical to SEQ ID NO:4. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs are encompassed within the scope of these claims,

Art Unit: 1652

including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1, 6-8, 10, 31, 35, 36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to a genus of DNA molecules comprising any DNA which is 95% identical to SEQ ID NO:4 and further comprising 1) a replicon selected from certain genera of certain well known and less known bacteria such as *Roseobacter*, *Pseudogluconobacter* etc. and 2) temperature sensitive replicons, 3) expression control sequence, 4) terminator sequence, 5) ribosome binding site. The specification does not contain any disclosure of the structure of all DNA sequences comprising the above bacterial replicons, temperature sensitive replicons, expression control sequence, terminator sequence, ribosome binding site. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of having many different structures. Therefore, many structurally unrelated DNAs are encompassed within the scope of

Art Unit: 1652

these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-39 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-25 of U.S. Patent No. 6,503,748. An obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but an examined application claim is not patentably distinct from the reference claim, because the examined claim is either anticipated by, or would have been obvious over the reference claim.

Art Unit: 1652

See, e.g., *In re Berg*, 140 F.3d 1428,46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi* 759 F.2d 887,225 USPQ 645 (Fed. Cir. 1985). Although the conflicting claims are not identical, they are not patentably distinct from each other. Claims 1-39 of the instant application and claims 1-25 of the reference patent are both directed to nucleic acid molecules comprising a polynucleotide that is 95% identical to a nucleotide sequence of an endogenous plasmid contained in NRRL deposit No.B-30035 and vectors and host cells comprising said nucleic acid molecule. Among the nucleic acid molecules, vectors and host cells claimed in the instant application and in the reference patent a good number of nucleic acid molecules are identical to one another. The portion of the specification (and the claims) in the reference patent that supports the recited nucleic acid molecules includes embodiments (for example, polynucleotides hybridizing to endogenous plasmid contained in NRRL deposit No.B-30035) that would anticipate the claimed nucleic acid molecules in claims 1-39 herein. Claims of the instant application listed above cannot be considered patentably distinct over claims 1-25 of the reference patent when there is specifically recited embodiment that would anticipate claims 1-39 of the instant application. Alternatively, claims 1-39 cannot be considered patentably distinct over claims 1-25 of the reference patent when there is specifically disclosed embodiment in the reference patent that supports claims 1-25 of that patent and falls within the scope of claims 1-39 herein because it would have been obvious to one having ordinary skill in the art to modify claims 1-25 of the reference by selecting a specifically disclosed embodiment that supports those claims i.e., for example, it would have been obvious to those skilled in the art to select the plasmid of NRRL deposit No. B-30035 or to select a polynucleotide having 95% identity thereto. Each of these polynucleotides

Art Unit: 1652

anticipate the claims of the instant application. One of ordinary skill in the art would have been motivated to do this because that embodiment is disclosed as being a preferred embodiment within claims 1-25 of the reference patent.

In response to the previous Office action, applicants have traversed the above rejection arguing that the US 6,503,748 and the instant application are not commonly owned and that the Examiner is mistaken that a TD will overcome the above rejection. Applicants also argue that the Examiner has not established a *prima facie* case and the argument is merely conclusory and rests on the proposition that claims to a genus are necessarily patentably indistinct over a narrower claim in the context of obviousness-type double patenting and that such a proposition is without merit. Applicants also assert that the instant application claims are patentably distinct and non-obvious over the claims in the '748 patent as that patent does not disclose or even suggest the SEQ ID NO:4 or certain fragments thereof comprise a replicon sequence thereof capable of autonomous replication in *Ketogulonigenium*. Applicant argues that absent applicant's guidance the skilled artisan would not have predicted that SEQ ID NO:4 or certain fragments thereof removed from endogenous *Ketogulonigenium* plasmid and joined to heterologous nucleic acid would confer on the heterologous nucleic acids the property of autonomous replication.

Examiner respectfully disagrees with all the above arguments by the applicant to be persuasive to overcome the above rejection. First of all, Examiner would like to make it clear to the applicants that he has made no mistake in concluding that the instant application and the reference patent have a common assignee. While the patent is co-owned by ADM and Michigan State University as indicated on the patent, Office records indicate that the instant application is

Art Unit: 1652

assigned to ADM. Furthermore, the reference patent and the instant application claim the benefit of the same provisional application 60/194,625 owned by ADM. Therefore, contrary to applicant's conclusion the instant application and the reference patent have a common assignee.

Applicant's argument that the rejection is merely conclusory and rests on the proposition that claims to a genus are necessarily patentably indistinct over a narrower claim is without merit, is not agreed with. As stated in the rejection above, the Federal Circuit has stated that a claim is not patentably distinct from a reference claim if the examined claim is anticipated or obvious over the reference claim. Thus an examined claim that fully encompasses an issued narrower claim (i.e., anticipation) is necessarily patentably indistinct therefrom. Applicant should note that the instant claims are not limited only to fragments of the endogenous plasmid of NRRL B-30035, but encompass the entire plasmid and variants thereof also. These have been previously patented and thus the patent claims anticipate the instant claims. Claims limited to SEQ ID NO:4 (i.e., polynucleotide consisting of SEQ ID NO:4 instead of comprising of SEQ ID NO:4) or other specific fragment might be patentably distinct from the patented claims, but the instant claims are not so limited. Hence for all the above reasons the rejection is maintained.

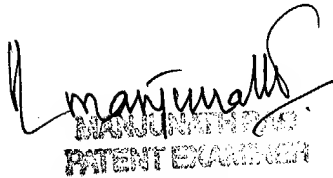
Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 703-306-5681. The examiner can normally be reached on 7.30 a.m. to 4.00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura

Art Unit: 1652

Achutamurthy can be reached on 703-308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-306-0196.



Manjunath N. Rao
December 12, 2003